A Prospective Study of Adverse Drug Reactions to Antiretroviral Therapy in a Tertiary Care Hospital at Allahabad, Uttar Pradesh

Arkapal Bandyopadhyay[1], Rakesh Chandra Chaurasia[2], Rakesh Kumar Yadav[3], Sarika Palepu[4]

ABSTRACT

Introduction: Human Immunodeficiency Virus has a significant disease burden globally. India has a large proportion of the global HIV infected patients. The state of Uttar Pradesh had 7500 new cases in 2015. Antiretroviral therapy is the cornerstone of treatment of HIV. These drugs are highly toxic and lead to diverse adverse drug reactions. The present prospective study was done to study the occurrence of adverse drug reactions and analyse the associated factors.

Material and Methods: The present study was conducted at Antiretroviral Therapy Centre, Swarup Rani Nehru Hospital at Allahabad, Uttar Pradesh. Patients were enrolled for two months and followed up monthly over a period of six months. A pretested interview schedule was administered to the study subjects. Information regarding socio-demographic profile, drug regimen and occurrence of adverse drug reactions was collected. Causality assessment was done by Naranjo's criteria. Bivariate and multivariate logistic regression was done to analyse the association of selected variables with the occurrence of adverse reactions.

Results: This study enrolled 163 participants and 152 participants completed the study. During the study period, 94 participants reported occurrence of at least one ADR. A total of 334 ADRs were reported among them. TLE regimen constituted 66.4% of adverse reactions. Central nervous system was most commonly involved (34.4%). By Naranjo's scale, majority of ADRs (61.6%) were categorised as "possible". Multi-variate analysis showed statistically significant association of occurrence of ADR with higher clinical staging of the patient.

Conclusion: Tenofovir based regimen was most commonly associated with ADRs. Rigorous monitoring is essential to prevent future events and improve safety.

Key words: Adverse Drug Reactions, Anti-retroviral Therapy, HIV, ART, Uttar Pradesh

INTRODUCTION

Human immunodeficiency virus (HIV) infection and acquired immune deficiency syndrome (AIDS) is a spectrum of conditions caused by an infection with a retrovirus known as the human immunodeficiency virus (HIV).[1] The first reported case of HIV was by United States Centre of Disease Control on 5th June, 1981.[2] Since then it has been a growing killer, affecting a large population globally. The Joint United Nations Programme on HIV/AIDS (UNAIDS) reported that AIDS should be considered as pandemic.[3]

Globally 36.9 million people were living with HIV (PLHIV) by the end of 2017. Sub-Saharan countries had the highest burden with 25.8 million PLHIV. Asia had 5 million PLHIV and has seen a 31% decline in new HIV infections between 2000 and 2014. India, China and Indonesia accounted for 78% of new HIV infections in the asian region. In 2017, deaths due to HIV related illness was 0.94 million. Globally, 21.7 million PLHIV were accessing antiretroviral therapy by December 2017.[4,5]

India has a large proportion of the global HIV infected patients. The first case of HIV infection in India was detected among female sex workers in Chennai, Tamil Nadu in 1986. In 1987, National AIDS Control Programme (NACP) was launched for integrating surveillance, blood screening and health education.[5,6] National AIDS Control Organization (NACO) was set up to look after the formulation of policies, prevention work and control programme relating to HIV and AIDS.[7] In the same year, Strategic Plan for HIV prevention established the administrative and technical basis for programme management and also set up State AIDS bodies in 25 states and 7 union territories.

According to the current scenario of HIV prevalence in India, it was estimated that national adult prevalence in 2015 would be 0.26% (0.3% in males and 0.22% in females). The prevalence was estimated to show a steady decline. The total number of PLHIV in India was estimated at 21.1 lakhs.[8] During the same period, an estimated 67.6 thousand people died of AIDS-related causes. Nevertheless, India has successfully achieved the 6th Millennium Development Goal of halting and reversing the HIV epidemic.[9,10]

Antiretroviral Therapy (ART) is cornerstone of treatment of HIV. It is often known as "Highly active antiretroviral therapy" or "HAART". ARV drugs are highly toxic and lead

[1]Senior Resident, Department of Pharmacology, All India Institute of Medical Sciences, Raipur, Chhattisgarh, [2]Professor, Department of Pharmacology, Moti Lal Nehru Medical College, Allahabad, Uttar Pradesh, [3]Assistant Professor, Department of Medicine, Moti Lal Nehru Medical College, Allahabad, Uttar Pradesh, [4]Senior Resident, Department of Community Medicine and Family Medicine, All India Institute of Medical Sciences, Bhubaneswar, Odisha

Corresponding author: Arkapal Bandyopadhyay, Senior Resident Room, Department of Pharmacology, Medical College, All India Institute of Medical Sciences, Tatibandh, Raipur, Chhattisgarh, India

How to cite this article: Arkapal Bandyopadhyay, Rakesh Chandra Chaurasia, Rakesh Kumar Yadav, Sarika Palepu. A prospective study of adverse drug reactions to antiretroviral therapy in a tertiary care hospital at Allahabad, Uttar Pradesh. International Journal of Contemporary Medical Research 2018;5(11):K1-K6.

DOI: http://dx.doi.org/10.21276/ijcmr.2018.5.11.9

to diverse adverse drug reactions (ADR). Significant distress to the patients caused by ADRs result in withdrawal of the offending drug or discontinuation of the treatment in many which ultimately result in a treatment failure. Surveillance mechanisms dealing with the occurrence of ADRs are lacking in the country.[11,12] Analyzing the causative factors and planning remedial measures to curb such ADRs is the need of the hour. Hence the present study was done to assess the adverse drug reactions among patients attending ART centre at SRN Hospital, Allahabad.

MATERIAL AND METHODS

The objectives were to study the adverse drug reactions in patients receiving Antiretroviral therapy in a tertiary care hospital at Allahabad, Uttar Pradesh and to study the association between selected variables and occurrence of adverse drug reactions.

The study protocol was presented to the Institutional Ethical Committee of Moti Lal Nehru Medical College, Allahabad. Following the approval, the study was conducted in the ART centre in a tertiary care hospital- Swarup Rani Nehru Hospital. The study period which was planned for eight months comprised two months of inclusion period and subsequent follow-up of six months. The study centre was visited twice a week (Monday and Thursday) during 9 am to 1 pm. The selection of patients was done following systematic random sampling method. Every third patient visiting the ART centre on these designated days were considered for inclusion in the study. Inclusion criteria included that the patients be registered to the ART centre and on ART regimen and who were willing to participate and gave consent. All patients irrespective of duration of ART were considered for inclusion. Participants who were seriously ill, suffering from psychiatric disorders and who could not comprehend interview questions were excluded from the study. A written informed consent was taken from the patient and an attendant in a local language (Hindi). Assent was taken from parents/ caregivers in participants who were below 18 years of age.

After initial enrollment into the study each patient was interviewed for 30-40 minutes in pre-tested semi structured interview schedule. Socio-demographic details,detailed clinical history and past laboratory data were collected. The patients who were already receiving ART before start of the study were enquired about their initial drug regimen details. The patient registration card issued by the hospital as per NACO guidelines was thoroughly checked for CD4 counts, changes in regimen and any adverse reactions. Each study participant was then given a card containing a unique identification code, date of follow up visit and the investigator's contact number to contact if there is any emergency during or after the study period. All norms of confidentiality were strictly maintained and followed.

During the follow up period, in every patient with suspected adverse event, a detailed drug history including drugs used during the 3 weeks preceding the adverse reaction, route of administration, dosage, concomitant medical products if any including self-medication and herbal remedies, duration of treatment, improvement after discontinuation of drug, purpose of taking the drug, whether prescribed or over-the-counter drug were noted. A detailed drug reaction history was noted. Grading of the ADRs was done according to standard guidelines of WHO. The WHO- ADR probability scale and Naranjo's algorithm were used for causality assessment of the ADRs. Severity of the ADR was assessed by Modified Hartwig and Siegel Scale. Preventability of ADR was assessed by Modified Shummock and Thornton Scale. In this study, Adverse Drug Reaction is defined as any response to a drug which is noxious and unintended, and which occurs at doses normally used in man.

Statistical methodology: Following the collection of data, it was entered using Epi info 7.1 and statistical analysis was done using STATA 14 and SPSS 22. Association of occurrence of ADRs with various determinants was studied. Bi-variate analysis was done with selected determinants and ADR occurrence using chi square test. Variables which were found to be significant (at $p<0.5$) were considered for inclusion in multi-variate analysis. A model for multi-variate logistic regression was developed with selected significant variables on bi-variate analysis. Multi-variate logistic regression was performed with the outcome variable as occurrence of ADR (coded as binary). For, multi-variate logistic regression technique, variables with $p<0.05$ were considered significant.

The trial was registered with Clinical Trial Register of India-CTRI/2018/02/012138.

RESULTS

A total of 170 patients were approached in the study. As 7 patients did not meet the inclusion criteria of the study they were excluded. Baseline interview schedule was administered among 163 patients. During the course of the study 11 patients were lost to follow-up. Hence the present prospective study was conducted among 152 patients. There were 86 males and 66 females in the study. Details of the socio-demographic characteristics of the study participants are given in table-1.

In the present study 28 patients had concurrent co-morbidities. Hepatitis B was positive in 2 patients and 26 patients had tuberculosis and were on treatment. It was seen that 115(75.4%) participants had history of contact, 22(14.4%) had a mother to child transmission, 13(8.6%) had a history of blood transfusion and 2(1.6%) patients had history of intravenous drug abuse.

Among the study participants there was a median delay of 5.5 days from the detection of HIV status to initiation of A.R.T. However there was a wide range of delay from 0 days to 7.9 years. Almost half of the participants (49.3%) had a CD4 counts > 250µL at the time of initiation of A.R.T. Majority of participants (66.4%) were on TLE followed by ZLN (12.5%), ALN (10.5%), ZLE (4.6%), ALE (2.6%), TLE, TLN and SLN comprised 0.7% each and Atazanavir, Lopinavir and Ritonavir combination comprised of 2.3%. It was seen that 52 patients had changes in their ART regimen during their treatment. While enquiring about the

Age group (in years)	Male N (%) (n=86)	Female N (%) (n=66)	Total N (%) (n=152)
0-10	11 (12.8)	5 (7.6)	16 (10.5)
11-20	9 (10.5)	5 (7.6)	14 (9.2)
21-30	11 (12.8)	18 (27.2)	29 (19.1)
31-40	34 (39.5)	18 (27.2)	52 (34.2)
41-50	16 (18.6)	15 (22.8)	31 (20.4)
51-60	4(4.7)	4(6.1)	8 (5.3)
>60	1(1.1)	1(1.5)	2(1.3)
Marital Status	**Male N (%)**	**Female N (%)**	**Total N (%)**
Married	53 (61.7)	33 (50.0)	86 (56.6)
Unmarried	28 (32.5)	10 (15.1)	38 (25.0)
Divorced/Separated	0 (0)	4 (6.1)	4 (2.6)
Widow/Widower	5 (5.8)	19 (28.8)	24 (15.8)
Education	**Male N (%)**	**Female N (%)**	**Total N (%)**
Illiterate	20 (23.2)	34 (51.5)	54 (35.6)
Primary School Completed	21 (24.4)	11 (16.6)	32 (21)
Middle School Completed	24 (28)	14 (21.2)	38 (25)
High School Completed	12 (14)	3 (4.6)	15 (9.8)
Intermediate or Post-School Diploma	2 (2.3)	1 (1.5)	3 (2)
Graduation or PG completed	7 (8.1)	3 (4.6)	10 (6.6)
Occupation	**Male N (%)**	**Female N (%)**	**Total N (%)**
Professional/Semi-professional	2 (2.3)	0 (0)	2 (1.2)
Clerk, Shop-keeper, Farmer	18 (20.9)	1 (1.5)	19 (12.5)
Skilled worker	6 (7.0)	2 (3.0)	8 (5.3)
Semi-skilled worker	14(16.3)	2 (3.0)	16 (10.6)
Un-skilled worker	20 (23.3)	19 (28.9)	39 (25.6)
Unemployed/Student	26 (30.2)	13 (19.7)	39 (25.6)
Home-maker	0	29 (43.9)	29 (19.2)

Table-1: Socio-demographic characteristics of the study participants

System	Number of ADRs	Frequency (%)
Central Nervous system	115	34.4
Gastro-intestinal system	65	19.5
Dermatology	52	15.6
Musculo-skeletal system	46	13.7
Laboratory abnormalities	44	13.2
Miscellaneous	7	2.1
Cardio-vascular system	5	1.5
Total	334	100.00

Table-2: System-wise ADRs among study participants

improvement in health condition, a significant proportion of patients (94.7%) claimed a positive response to ART. About 96% of the participants have received advice regarding the possible adverse drug reactions from the healthcare personnel. A similar proportion of patients (96%) were aware of the ADRs from ART regimens.

Among the study participants, 62% (94 participants) reported at least one adverse drug reaction during follow up. There were a total of 334 adverse drug reactions among these 94 participants. A total of 175 ADRs were reported in 44 females and 159 ADRs were reported in 50 males. The maximum number of ADRs reported in a participant was 10. Various ADRs in the study participants are enumerated below in Table-2. TLE constituted 66.9% of total ADRs followed by ZLN (14.6%), ALN (6.9%), ZLE (2.8%), TLN (2.5%), Atazanavir combination (2.5%), ALE (1.9%), SLE (1.0%) and SLN (1.0%). However there was no significant difference found in the occurrence of ADRs with various ART regimens. Details of system-wise ADRs with various ART regimens are given in Table-3

Most common CNS ADRs were associated with peripheral neuropathy (n=24, 20.9%). Nausea and vomiting (n=22, 33.8%) were the commonest symptoms associated with gastrointestinal system. Dermatologic ADRs were mostly in the form of skin rashes (n=20, 38.8%). Musculo-skeletal system was involved in 46 ADRs. Most commonly seen adverse effect was weakness (n=23, 50%).

The causality assessment done by WHO-UMC scale showed that 1.2% ADRs were certain, 39.8% ADRs were Probable/ Likely, 56.7% ADRs were Possible and 2.3% ADRs were Unlikely. When causality assessment was done by Naranjo's algorithm 1.2% ADRs were Definite, 37.2% were Probable and 61.6% were Possible. Severity Assessment done by Modified Hartwig and Siegel Scale showed 58.1% of ADRs were of mild severity, 38.3% ADRs was of moderate severity and 3.6% ADRs were of severe nature. Preventability

System	TLE	ZLN	ZLE	SLN	TLN	ALN	ALE	SLE	Others	Total
Gastro-intestinal	44	13	0	3	1	2	1	0	1	65
Dermatology	27	5	6	0	0	9	2	0	3	52
Central Nervous	89	8	3	2	5	4	0	2	2	115
Musculo-skeletal	34	8	0	0	2	0	0	1	1	46
Cardio-vascular	2	2	0	0	0	0	0	0	1	5
Miscellaneous	5	2	0	0	0	0	0	0	0	7
Lab abnormalities	22	10	0	1	0	8	3	0	0	44
Total	223	48	9	6	8	23	6	3	8	334

Table-3: System wise ADRs with different ART regimens

Variable	Category	Adverse Drug Reactions		Odds ratio (95% CI) p-value (Unadjusted)	Odds ratio (95% CI) p-value (Adjusted)
		No	Yes		
Age	≤35	33	46	1	-
	>35	25	48	1.37 (0.67 – 2.80) 0.34	1.07 (0.49-2.31) 0.86
Sex	Female	22	44	1	-
	Male	36	50	0.69 (0.33-1.42) 0.28	0.66 (0.31-1.41) 0.29
Co-morbidities	No	52	72	1	1
	Yes	6	22	2.64 (0.94-8.50) 0.04	0.57 (0.26-1.25) 0.65
Education	Illiterate	15	39	1	-
	Literate	43	55	0.49 (0.22-1.06) 0.05	0.54 (0.23-1.28) 0.16
CD4 count	≤250	32	45	1	-
	>250	26	49	1.34 (0.66-2.72) 0.38	1.60 (0.78-3.29) 0.19
Delay in treatment	Delay	36	57	1	-
	No delay	22	37	1.06 (0.51-2.20) 0.86	-
Clinical staging	1,2	48	53	1	-
	3,4	10	41	3.71 (1.59-9.17) 0.0008	4.42 (1.55-12.60) 0.005
Adherence	Good	14	35	1	1
	Bad	44	59	0.53 (0.23-1.17) 0.09	0.57 (0.26-1.25) 0.16

For analysis,
1. Clinical staging was classified into two categories. Category 1 comprised of stage 1,2 and category 2 comprised of stage 3,4.
2. Bad Adherence - A patient missing atleast one dose in the past one week is considered as non-adherent

Table-4: Association of various variables with occurrence of adverse drug reactions

assessment done by Modified Shummock and Thornton scale showed that ADRs were definitely preventable in 11.5% patients, probably preventable in 74.6% patients and not preventable in 13.9% patients.

To study the factors affecting the association of categorical variables with ADR, bivariate followed by multivariate regression test was done. Age, sex, CD4 count, education, delay in treatment, clinical staging and adherence were compared with ADR occurrence. There was statistically significant association between higher clinical staging and increased odds of occurrence of ADRs on multivariate analysis. (OR-4.42, 95% CI= 1.55-12.60, P value=0.005). (Table-4)

DISCUSSION

The present study enumerates the adverse effects of ART

regimen. The median age of the study participants was 35 with range of 21-40 years. This was similar as observed by Bhuvana et al[13] and Reddy et al.[14] Majority of the participants (35.6%) were illiterate as observed in these two studies. A median delay of 5.5 days from the detection of HIV status to initiation of A.R.T was seen among the participants. A study by Thuppal et al[15] showed a median delay of 36 days with TDF regimen and 116 days with AZT based regimens.

Incidence of ADRs accounted to 4.4 per person year and incidence of ADR reporting individuals to 123 per 100 person years. Different studies reported incidence as 59 per 100 person-years (70.8 per 1000 person-months) by Santini et al[16] and 52 per 100 person-years by Shet et al.[17] Different regimens of ART and duration of study period in these studies might have contributed to lower incidence.

Tenofovir based regimen TLE constituted 223 (66.9%) of total ADRs followed by other regimens. Studies with TDF based regimen as first line therapy in Indian population are scarce. A study by Thuppal et al[15] at Vellore contradicted the present study findings showing more ADR with AZT based regimen. Factors as better socioeconomic condition, age profile, less delay time between diagnosis and initiation of treatment than patients on the AZT-containing regimen and inclusion of only new patients might attribute to the differences observed.

Among our study participants, 94 participants (62%) reported at least one adverse drug reaction during the study period of six months. The maximum number of ADRs reported in a participant was 10. A study by Vaghani et al (60.8%)[18] and Sreenivasan et al (60%)[19] had similar incidences whereas study by Shet et al (90.1%),[17] Nagpal et al (90.6%),[20] Harminder et al (86.2%)[21] had higher incidences of ADRs. The duration of study period was different in these studies compared to the present study.

Another contradictory feature was that majority of patients in these two studies were on SLN and ZLN regimen therapy, accounting for more ADRs than the present study. Studies by Srikanth et al (34.1%)[22] and Reddy et al (31%)[14] had a lower incidence of ADR among study participants. Our present study was prospective unlike the above studies (which were retrospective) and might have contributed to less recall bias and higher incidence of ADRs. In the study females (n=175) presented with more ADR than men (n=159), but the difference was not statistically significant. A similar result of higher prevalence in females was observed in studies done by Diwakar et al[23] and Harminder et al.[21] Central nervous system was most commonly involved with 115 (34.4%) ADR as observed in other studies by Harminder et al and Vaghani et al.[18]

Causality assessment of the present study shows similar result as reported by Reddy et al[14] and Khan et al.[24] Severity assessment showed similar observation as done by Vaghani et al[18] and Bhuvana et al.[13] Preventability assessment results in the present study was similar to Rajesh et al[25] and Bhuvana et al.[13]

The association of the variables with occurrence of ADRs in the present study showed that clinical staging at the time of diagnosis was significantly associated with the occurrence of ADRs. A similar observation was shown by Diwakar et al.[23]

The strength of this study lies in being a prospective observational study. Moreover, it was the first of its kind in M.L.N Medical College, Allahabad, Uttar Pradesh representing the population of northern part of India. High response rate was seen in the study and loss to follow up was minimal enabling for more precise results. The participants were followed for a period of six months, which is a significant time for observing ADRs. The study included patients of all age groups. Currently, TLE has become the first line ART and this study had observed its adverse effects along with other existing regimens. The study was based on the drugs given free of cost by the Indian National ART programme conducted by NACO and has a public health relevance nationally. However, the study has few limitations. The sample size of the study was small. There is also substantial difference in number of participants in different ART regimens. It was based on a sample from a single ART centre in Allahabad questioning the representativeness. As patients both previously and newly diagnosed were included, those on ART from a long time could have already had some form of ADRs before enrolment into the present study which were not taken into account. Also, misclassification of cause of ADR and causality assessment was a possibility.

CONCLUSION

The present study explains the burden of adverse drug reactions among patients attending ART centre at S.R.N hospital, Allahabad. It is seen that perceived adverse drug reactions due to antiretroviral therapy are very frequent and prevalent in the sampled population. Hence, diverse monitoring strategies should be implemented in the medical system to diagnose adverse drug events and address them at the earliest. A better ascertainment of the timing of clinically important adverse events would help in defining the monitoring requirements. Advanced research methods to rationalize toxicity monitoring are the need of the hour.

REFERENCES

1. Kagaayi J, Serwadda D. The History of the HIV/AIDS Epidemic in Africa. Curr HIV/AIDS Rep. 2016;13:187-93.
2. Weiss RA. How does HIV cause AIDS?. Science. 1993; 260: 1273–9.
3. Gottlieb MS. Pneumocystis pneumonia--Los Angeles. 1981. Am J Public Health. 2006; 96: 980–83.
4. Data and Statistics, World Health Organization, Available at http://www.who.int/hiv/data/en/. Last accessed on 10th September, 2018.
5. UNAIDS FACT SHEET 2017, Global Statistics. Available at- http://www.unaids.org/en/resources/fact-sheet. Last accessed on 10th September, 2015.
6. Solomon S, Solomon SS, Ganesh AK. AIDS in India. Postgrad Med J. 2006;82:54 5-7.
7. Kakar D.N. and Kakar S.N. Combating AIDS in the 21st century, Issues and Challenges. Sterling Publishers Private Limited, p.31.
8. Bhupesh M. 'India Disquiet About AIDS Control'. The

Lancet,1992; Vol240, No.8834/8 835.

9. HIV/AIDS in India. Accessed from: http://www.aidsdatahub.org/Country-Profiles/India Last accessed-12th June 2017.
10. HIV and AIDS estimates (2015). Available at: http://www.unaids. org/en/regions countries/countries/india. Last accessed 4th July, 2017.
11. Hawkins T. Understanding and managing the adverse effects of antiretroviral therapy. Antiviral Res. 2010; 85:201-9.
12. Annual Report 2015-2016, NACO. Available at http://www.naco.gov. in/sites/default/files/Annual%20Report%202015-16_NACO.pdf. Last accessed on 6th Sep, 2016.
13. Bhuvana KB, N. G. Hema NG, Sangeetha. A prospective observational study of adverse drug reactions to antiretroviral therapy: type and risk factors in a tertiary care teaching hospital. Int J Basic Clin Pharmacol. 2014; 3:380-384.
14. Reddy AV, Lihite RJ, Lahkar M, Choudhury U. A study on adverse drug reactions in hiv infected patients at a art centre of tertiary care hospital in guwahati, India. Asian J Pharm Clin Res. 2013; (Suppl 2):102-104.
15. Thuppal SV, Wanke CA, Noubary F, et al. Toxicity and clinical outcomes in patients with HIV on zidovudine and tenofovir based regimens: a retrospective cohort study. Trans R Soc Trop Med Hyg. 2015; 109: 379–385.
16. Santini OM, Friedman RK, Veloso VG, Cunha CB, Pilotto JH, Marins LM et al. Incidence of antiretroviral adverse drug reactions in pregnant women in two referral centers for HIV prevention of mother-to-child-transmission care and research in Rio de Janeiro, Brazil. Braz J Infect Dis. 2014; 18:372-8.
17. Shet A, Antony J, Arumugam K, Kumar Dodderi S, Rodrigues R, et al. Influence of Adverse Drug Reactions on Treatment Success: Prospective Cohort Analysis of HIV-Infected Individuals Initiating First-Line Antiretroviral Therapy in India. PLoS ONE 2014;9: e91028.
18. Vaghani SV, Gagiya AK, Shukla DK, Patel VP. Adverse effects of antiretroviral treatment at a tertiary care hospital in India: a prospective observational study. Int J Res Med Sci. 2013;1:230-32.
19. Srirangaraj S, Venkatesha K. Adverse effect after HAART Initiation in resource limited settings, a prospective study from Mysore, India. J Infect Dev Ctries. 2010; 4:750-3.
20. Nagpal M, Tayal V, Kumar S, Gupta U. Adverse drug reactions to antiretroviral therapy in aids patients at a tertiary care hospital in India: A prospective observational study. Indian J Med Sci. 2010; 64:245-52.
21. Singh H, Dulhani N, Tiwari P, Singh P, Sinha T. A prospective, observational cohort study to elicit adverse effects of antiretroviral agents in a remote resource-restricted tribal population of Chhattisgarh. Indian J Pharmacol. 2009; 41:224-226.
22. Srikanth BA, Babu SC, Yadav HN, Jain SK. Incidence of adverse drug reactions in human immune deficiency virus-positive patients using highly active antiretroviral therapy. J Adv Pharm Tech Res. 2012; 3:62-7.
23. Divakar B, Mistry SD, Kantharia ND, Mamtarani. The Study Of Adverse Drug Reactions (Adr's) In Hiv Patients Taking Highly Active Antiretroviral Therapy In Art Centre, Nch, Surat, India.IJMPS. 2012;3: 9-18.
24. Khan K, Khan AH, Sulaiman SA, Soo CT, Akhtar A. Adverse Drug Reactions in HIV/AIDS Patients at a Tertiary Care Hospital in Penang, Malaysia. Jpn. J. Infect. Dis. 2012; 69:56–59.
25. Rajesh R, Sudha V, Varma D, Sonika S. Association between Medication Adherence Outcomes and Adverse Drug Reactions to Highly Active Antiretroviral Therapy in Indian Human Immunodeficiency Virus-Positive Patients. JYP. 2012; 4:250-60.

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 11-10-2018; **Accepted:** 04-11-2018; **Published:** 15-11-2018